REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested in light of the remarks which follow.

I. Claim Amendments

Claims 1 and 5 have been amended to recite "concurrently introducing the transgene and an insulator from sea urchin arylsulfatase into an animal or a plant, organs of an animal or a plant, or cells derived from an animal or a plant." This amendment is supported in the specification at page 8, first full paragraph, which indicates that the transgene "may be introduced into living bodies, organs of the living body, and cells derived from the living body," where "the living body" means "any animal or plant."

New dependent claims 27 and 28, directed specifically to animals and humans, have been added.

These amendments are supported in the original claims. No new matter has been added, and Applicants respectfully request entry of these amendments.

IV. Response to Claim Rejections Under 35 U.S.C. §§ 102 and 103

A. Claims 1-8 and 17-19 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Hino et al. (Blood, 2002 November 16, Vol. 100, No. 11, pp. Abstract No. 5522).

Specifically, the Examiner has stated that Hino et al. describes a method to protect a transgene from silencing by introducing a lentiviral vector comprising an insulator from sea urchin arylsufatase, Arsl, into HL-60 cells in both sense and antisense orientations.

In response, Applicants submit herewith a Declaration Under 37 C.F.R. § 1.132 establishing that Hino et al. describes the present inventors' own work. In particular, the named inventors of the present application (Masao Matsuoka and Koji Akasaka) are co-authors of Hino et al., along with additional co-authors (Shinjiro Hino, Pan Jun, and Shuhei Taguwa). As stated in the Declaration, the named inventors are the only inventors of the invention claimed in the present application and described in Hino et al., and the additional co-authors of the reference were merely working under the direction and supervision of one of the named inventors.

Accordingly, Hino et al. does not qualify as prior art under § 102(a) against the present application, and Applicants respectfully request reconsideration and withdrawal of this rejection.

B. Claims 1, 4, 5 and 8 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Shinmyo et al. (U.S. Patent 6,229,070). In addition, claims 2, 3, 6, 7 and 17-20 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Shinmyo et al.

Specifically, the Examiner has stated that Shinmyo et al. discloses a method for introducing a transgene into a plant cell concurrently with ArsI, wherein expression of the transgene is stabilized and more uniform than without the insulator. According to the Examiner, the insulator can be introduced in both the sense or the antisense orientations. The Examiner also indicated that although Shinmyo et al. do not teach the claimed method wherein the transgene is introduced using a viral vector such as the lentiviral vector, lentiviral vectors are well known in the art and routinely used for introducing transgenes into cells.

Applicants respectfully traverse the rejections over Shinmyo et al. for at least the following reasons.

The most prominent feature of this invention lies in the finding that ArsI has an anti-silencing effect. In contrast, Shinniyo et al. does not teach or suggest that ArsI could be useful in methods for protecting a transgene from silencing. Therefore, the

methods recited in the present claims are not anticipated by or obvious over Shinmyo et al.

It is generally recognized that an insulator is a DNA sequence that ensures stable gene expression, independent of environmental conditions, by exerting enhancer blocking effects and inhibiting position effects. Therefore, an insulator is defined as a DNA sequence that has either one or both of these effects, as disclosed in paragraphs [0007] and [0008] of the present specification.

However, it is also known that an anti-silencing effect is not an indispensable requirement of an insulator. Therefore, although Shinmyo et al. discloses that ArsI can serve as an insulator, a person of ordinary skill in the art would not have reasonably expected that ArsI would possess anti-silencing activity.

To support the argument regarding the unpredictability of anti-silencing effect, Applicants submit herewith the results of investigations on enhancer blocking effect and anti-silencing effect obtained by using other insulators (HCF1 and 5-32) and a DNA fragment lacking a region of ArsI (Dfrag.6). The DNA fragments of HCF1 and 5-32 are insulators derived from human, which are known to exert enhancer blocking effects in sea urchin embryos.

In the experiments submitted herewith, an anti-silencing effect can be demonstrated by a change in the percentage of EGFP (Enhanced Green Fluorescence Protein) positive cells. As shown in the graph in attachment 1, the percentage of EFGP positive cells was the same in the presence (HCF1+) or absence (HCF1-) of HCF1. Thus, HCF1 does not exhibit an anti-silencing effect. In contrast, as shown in the graphs in attachment 2, the time course of EFGP positive cells (right graph) and the average fluorescence intensity (left graph) differed in the presence (5-32+) as compared to the absence (5-32-) of 5-32. Thus, 5-32 exhibits both anti-silencing effect and enhancer blocking effect.

Moreover, anti-silencing and enhancer blocking effects were investigated using a DNA fragment lacking a part of ArsI (i.e. Dfrag.6) (attachment 3). The nucleotides deleted in Dfrag.6 are represented by red-colored nucleotides in the

figure on the left. As shown in the data represented in the right upper graph of attachment 3, the time-dependent decrease in the percentage of EFGP positive cells (control) was significantly inhibited by the presence of Dfrag.6. Thus, the anti-silencing effect is maintained regardless of the deficiency in the red-colored nucleotides. However, as shown in the data represented in the figure shown in the right lower graph of attachment 3, the enhancer blocking effect was lost in Dfrag.6.

The results described above are summarized in attachment 4. As can been seen from the table set forth in this attachment, HCF1 did not demonstrate anti-silencing effect, whereas 5-32 did. Moreover, as indicated from the results shown using Dfrag.6, a DNA fragment can lose its enhancer blocking activity while at the same time maintaining its anti-silencing effect. Thus, an insulator does not necessarily possess anti-silencing activity. Accordingly, Shinmyo et al. does not teach or suggest a method for protecting a transgene from silencing, and a person of ordinary skill in the art would not have reasonably expected, based on the disclosure of the reference, that ArsI could be used in the recited method.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the §§ 102 and 103 rejections.

III. Response to Claim Rejections Under 35 U.S.C. § 112

Claims 1-8 and 17-20 have been rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite.

Specifically, the Examiner stated that the claims are indefinite because it is not clear where the transgene and the insulator are introduced, whether into a cell, a plant, an animal, or "just a tube."

As noted above, claims 1 and 5 have been amended to clarify that the transgene and the insulator are introduced into "an animal or a plant, organs of an animal or a plant, or cells derived from an animal or a plant."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

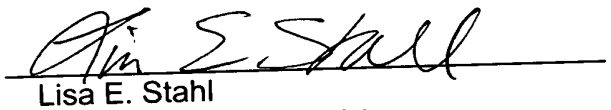
It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this paper, or the application in general, the Examiner is respectfully urged to telephone Applicants' undersigned representative so that prosecution of this application may be expedited.

Respectfully submitted,

BUCHANAN INGERSOLL PC

Date: October 31, 2006

By: 

Lisa E. Stahl
Registration No. 56,704

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620